AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

- 1. (currently amended): An aqueous composition comprising an amphiphilic block copolymer having a hydrophilic block and a hydrophobic block, dispersed in the solution, and a biologically active compound associated with the polymer, characterised in that wherein the hydrophilic block has pendant zwitterionic groups.
- 2. (original): A composition according to claim 1 in which the biologically active molecule is associated by hydrophobic interactions with the copolymer.
- 3. (currently amended): A composition according to claim 2 in which the biologically active compound has a measured and/or calculated partition coefficient between octanol and water, log P or clog P of at least 1.0, preferably at least 1.5.
- 4. (currently amended): A composition according to any preceding claim 1 in which the copolymer is dispersed in the form of micelles.
- 5. (currently amended): A composition according to any preceding claim 1 wherein the hydrophilic block is formed by radical polymerisation of ethylenically unsaturated monomers.
- 6. (original): A composition according to claim 5 in which the monomers comprise a zwitterionic monomer.
 - 7. (currently amended): A composition according to claim 6 in which the

zwitterionic monomer has the general formula

I

YBX

in which Y is an ethylenically unsaturated group selected from the group consisting of $H_2C=CR-CO-A-$, $H_2C=CR-C_6H_4-A^1-$, $H_2C=CR-CH_2A^2$, $R^2O-CO-CR=CR-CO-O$, RCH=CH-CO-O-, $RCH=C(COOR^2)CH_2-CO-O$,

A is -O- or NR^1 ;

 A^{1} is selected from the group consisting of a bond, $(CH_{2})_{I}A^{2}$ and $(CH_{2})_{I}SO_{3}$ - in which I is 1 to 12;

A² is selected from the group consisting of a bond, -O-, O-CO-, CO-O, CO-NR¹-, -NR¹-CO, O-CO-NR¹-, and NR¹-CO-O-;

R is hydrogen or C_{1-4} alkyl;

 R^1 is hydrogen, C_{1-4} alkyl or BX;

 R^2 is hydrogen or C_{1-4} , alkyl;

B is selected from the group consisting of a bond, or a straight and branched alkanediyl groups, alkylene oxaalkylene groups, or and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

X is a zwitterionic group.

8. (currently amended): A composition according to claim 7 in which X is a group

of the general formula II

in which the moieties A^3 and A^4 , which are the same or different, are -O-, -S-, -NH- or a valence bond, preferably -O-, and W⁺ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is preferably a C_{1-12} -alkanediyl group,

preferably in which W⁺ is a group of formula

-W⁺-N⁺R³₃, W⁺-P⁺R⁴₃, W⁺-S⁺R⁴₂-or W⁺-Het⁺ in which:

W¹ is alkanediyl of I or more, preferably 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted aryl (arylene), alkylene arylene, arylene alkylene, or alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or alkylene cycloalkyl alkylene, which group W¹ optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R³ are the same or different and each is hydrogen or alkyl of 1 to 4 carbon atoms, preferably methyl, or aryl, such as phenyl, or two of the groups R³ together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R³ together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each

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ring, and optionally one or more of the groups R³ is substituted by a hydrophilic functional group, and

the groups R⁴ are the same or different and each is R³ or a group OR³, where R³ is as defined above; or

Het is an aromatic nitrogen-, phosphorus or sulphur-, preferably nitrogen-, containing ring, for example pyridine.

9. (currently amended): A composition according to claim 7 in which X has the general formula III

where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4, in which preferably the groups R^5 are the same preferably methyl.

- 10. (currently amended): A composition according to any of claims 7 to 9claim 7 in which Y is H₂C=CR-CO-A- in which R is H or methyl and -A- is -O- or -NH-.
- 11. (currently amended): A composition according to any of claims 7 to 10claim 7 in which B is a C₂₋₆-alkanediyl group.
- 12. (currently amended): A composition according to any of claims 7 to 11claim 7 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.
 - 13. (currently amended): A composition according to any preceding claim 1 in

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which the hydrophobic block comprises pendant groups which are ionisable, having a p K_A or p K_B in the range 4 to 10, preferably in the range 5 to 9, for instance in the range 6 to 8.

- 14. (original): A composition according to claim 13 in which the hydrophobic block is formed by radical polymerisation of ethylenically unsaturated monomers.
- 15. (currently amended): A composition according to claim 14 in which the monomers from which the hydrophobic block is formed have the general formula VII

$$Y^1B^1Q$$
 VII

in which Y^1 is an ethylenically unsaturated group selected from the group consisting of $H_2C=CR^{40}-CO-A^8-$, $H_2C=CR^{14}-C_6H_4-A^9-$, $H_2C=CR^{14}-CH_2A^{10}$, $R^{16}O-CO-CR^{14}=CR^{14}-CO-O$, $R^{14}CH=CH-CO-O-$, $R^{14}CH=C(COOR^{16})CH_2-CO-O$,

 A^8 is -O- or NR^{15} ;

 A^9 is selected from the group consisting of a bond, $(CH_2)_qA^{10}$ and $(CH_2)_qSO_3$ - in which q is 1 to 12;

A¹⁰ is selected from the group consisting of a bond, -O-, O-CO-, CO-O-, CO-NR⁴¹-, -NR⁴¹-CO, O-CO-NR¹⁵-, and NR¹⁵-CO-O-;

 R^{14} is hydrogen or C_{1-4} , alkyl;

R¹⁵ is hydrogen, C₁₋₄- alkyl or B¹Q;

R¹⁶ is hydrogen or C₁₋₄ alkyl;

B¹ is <u>seletected from the group consisting of</u> a bond, or a straight <u>and branched alkanediyl groups</u>, alkylene oxaalkylene <u>groups</u>, or and alkylene (oligooxalkylene) group groups, optionally containing one or more fluorine substituents; and

Q is a cationic or cationisable group of the formula -NR¹⁷_P, -PR¹⁷_P and or SR¹⁷₁, in which p is 2 or 3, r is 1 or 2, the groups R¹⁷ are the same or different and each is selected from the group consisting of hydrogen, C₁₋₂₄ alkyl and aryl, or two of the groups R¹⁷ together with the heteroatom to which they are attached from a 5 to 7 membered heterocyclic ring or three R¹⁷ groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring, either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R¹⁷ groups may be substituted by amino or hydroxyl groups or halogen.

- 16. (original): A composition according to claim 15 in which Q is NR^{17}_2 in which each R^{17} is H or C_{1-4} -alkyl.
- 17. (currently amended): A composition according to claim 5-or claim 14 in which the ethylenically unsaturated monomers include comonomer.
- 18. (currently amended): A composition according to claim 17 in which the or each comonomer has the general formula VIII

in which R^{18} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{22}$ in which R^{22} is hydrogen and C_{1-4} alkyl;

R¹⁹ is selected from the group consisting of hydrogen, halogen and C₁₋₄ alkyl;

 R^{20} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{22}$ provided that R^{18} and R^{20} are not both $COOR^{22}$; and

R²¹ is a-selected from the group consisting of C₁₋₁₀ alkyl, a-C₁₋₂₀ alkoxycarbonyl, a-monoor di-(C₁₋₂₀ alkyl) amino carbonyl, a-C₆₋₂₀ aryl (including alkaryl) a-C₇₋₂₀ aralkyl, a-C₆₋₂₀ aryloxycarbonyl, a-C₁₋₂₀-aralkyloxycarbonyl, a-C₆₋₂₀ arylamino carbonyl, a-C₇₋₂₀ aralkyl-amino, a hydroxyl or aand C₂₋₁₀ acyloxy groupgroups, any of which may have one or more substituents selected from the group consisting of halogen atoms, and alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine (including mono and di alkyl amino and trialkylammonium in which the alkyl groups may be substituted), carboxyl, sulphonyl, phosphoryl, phosphino, (including mono and di alkyl phosphine and tri-alkylphosphonium), zwitterionic, hydroxyl-groups, vinyloxycarbonyl and other vinylic or allylic substituents, and reactive silyl or and silyloxy groups, such as trialkoxysilyl groups;

or R^{21} and R^{20} or R^{21} and R^{19} may together form -CONR²³CO in which R^{23} is a $C_{1\text{-}20}$ alkyl group.

19. (currently amended): A composition according to claim 18 in which the

comonomer is selected from the group consisting of a C₁₋₂₄ alkyl(alk)-acrylates, or-C₁₋₂₄-alkyl(alk)-acrylamides, mono-or-and di-hydroxy-C₁₋₆-alkyl(alk)-acrylamides, or-acrylamides, mono-and di-hydroxy-C₁₋₆-alkyl(alk) acrylamides, oligo(C₂₋₃ alkoxy) C₂₋₁₈ alkyl (alk)-acrylates, or-acrylamideC₂₋₁₈ alkyl(alk)acrylamides, styrene, vinylacetate or-and N-vinyllactam.

- 20. (currently amended): A composition according to any preceding claim 1 in which the polydispersity of molecular weight of each of the blocks is less than 2.0, preferably less than 1.5, more preferably in the range 1.1 to 1.4.
- 21. (currently amended): A composition according to any of claims 5 to 13claim 5 in which the degree of polymerisation of the hydrophilic block is in the range 2 to 1000, preferably 5 to 250, more preferably 10 to 100.
- 22. (currently amended): A composition according to any of claims 14 to 16 claim 14 in which the degree of polymerisation of the hydrophobic block is in the range 5 to 2000, preferably 10 to 500, more preferably 20 to 250.
- 23. (currently amended): A composition according to claim 21 or 22 in which the ratio of the degrees of polymerisation of the hydrophobic to hydrophilic blocks is in the range 1:5 to 10:1, preferably 1:1 to 5:1.
- 24. (original): A composition according to claim 5 in which the radical polymerisation is a controlled radical polymerisation.
- 25. (original): A composition according to claim 24 in which the polymerisation is an atom transfer radical polymerisation or group transfer polymerisation.
 - 26. (original): A composition according to claim 25 in which the initiator for the

radical transfer polymerisation process is a polymer compound in which the polymeric moiety is hydrophobic which forms the hydrophobic block of the copolymer.

- 27. (original): A composition according to claim 25 in which the hydrophobic block is also formed from ethylenically unsaturated monomers by a radical transfer polymerisation process.
- 28. (currently amended): A composition according to any preceding claim 1 in which the biologically active molecule is a cytotoxic compound, preferably an anti-cancer drug.
- 29. (currently amended): A method of forming an aqueous composition comprising an amphiphilic block copolymer and a biologically active compound, in which the copolymer comprises a hydrophilic block and a hydrophobic block in which process an aqueous dispersion of empty copolymer micelles is formed and the micellar dispersion is contacted with biologically active compound under conditions such that the biologically active compound becomes associated with the copolymer in the micelles, characterised in that wherein the hydrophilic block has pendant zwitterionic groups.
- 30. (currently amended): A method according to claim 29 in which the biologically active compound has a partition coefficient between octanol and water (log P) of at least 1.0, preferably at least 1.5, for instance 2.0 or higher.
- 31. (currently amended): A method according to claim 29 or claim 30 in which the hydrophobic block of the copolymer comprises ionisable groups, and in which the empty copolymer micelles are formed by a process comprising:
 - a) a first copolymer dissolution step in which the block copolymer, with the groups of

hydrophobic block in at least partially ionised form, is dissolved in an aqueous liquid, and

b) a second micelle forming step in which the conditions in the solution are adjusted so that the ionised groups are converted at least partially to their ionisable form, whereby the copolymer is above the critical micelle concentration in the aqueous liquid and micelles are formed.

- 32. (original): A method according to claim 31 in which the conditions which are adjusted are of temperature and/or pH.
- 33. (currently amended): A method according to claim 31-or 32 in which the ionisable groups are primary, secondary or tertiary amine groups and in which the micelle forming step involves raising the pH whereby the ionised groups become deprotonated.
- 34. (currently amended): A method according to any of claims 29 to 33 claim 29 in which the biologically active compound is in solid form when it is contacted with the aqueous dispersion of empty micelles.
- 35. (currently amended): A method according to any of claims 29 to 34 claim 29 in which the biologically active compound is in solution in an organic solvent when it is contacted with the aqueous dispersion of empty micelles.
 - 36. (canceled).
- 37. (new): A composition according to claim 3 in which the said partition coefficient is at least 1.5.
- 38. (new): A composition according to claim 8 in which W^+ is a group of formula $-W^1-N^+R^3$, $-W^1-P^+R^4$, $-W^1-S^+R^4$ or $-W^1-Het^+$ in which:

W¹ is selected from the group consisting of alkanediyl of 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene and alkylene cycloalkyl alkylene, which group W¹ optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R³ are the same or different and each is selected from the group consisting of hydrogen, alkyl of 1 to 4 carbon atoms and aryl or two of the groups R³ together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R³ together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R³ is substituted by a hydrophilic functional group, and

the groups R⁴ are the same or different and each is R³ or a group OR³, where R³ is as defined above; and

Het is an aromatic nitrogen-, phosphorus- or sulphur-containing ring.

- 39. (new): A composition according to claim 14 in which the ethylenically unsaturated monomers include comonomer.
- 40. (new): A composition according to claim 39 in which the comonomer has the general formula VIII

in which R^{18} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{22}$ in which R^{22} is hydrogen or C_{1-4} alkyl;

 R^{19} is selected from the group consisting hydrogen, halogen and C_{1-4} alkyl;

 R^{20} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{22}$ provided that R^{18} and R^{20} are not both $COOR^{22}$;

 R^{21} is selected from the group consisting of C_{1-10} alkyl, C_{1-20} alkoxycarbonyl, mono- or di-(C_{1-20} alkyl) amino carbonyl, C_{6-20} aryl, C_{7-20} aralkyl, C_{6-20} aryloxycarbonyl, C_{1-20} -aralkyloxycarbonyl, C_{6-20} arylamino carbonyl, C_{7-20} aralkyl-amino, hydroxyl and C_{2-10} acyloxy group, any of which may have one or more substituents selected from the group consisting of halogen atoms and alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine, carboxyl, sulphonyl, phosphoryl, phosphino, zwitterionic, hydroxyl, vinyloxycarbonyl, and reactive silyl and silyloxy groups,

or R^{21} and R^{20} or R^{21} and R^{19} may together form -CONR²³CO in which R^{23} is a $C_{1\text{-}20}$ alkyl group.

41. A composition according to claim 40 in which the comonomer is selected from the group consisting of C_{1-24} alkyl(alk)acrylates, C_{1-24} alkyl(alk)acrylamides, mono- and dihydroxy- C_{1-6} alkyl(alk)acrylates, mono- and dihydroxy- C_{1-6} -alkyl(alk)acrylamides, oligo(C_{2-3} alkoxy) C_{2-18} -alkyl(alk)acrylates, C_{2-18} alkyl(alk)acrylamides, styrene, vinylacetate and N-

vinyllactam acrylamides, mono- and di-hydroxy- C_{1-6} -alkyl(alk)acrylates, and acrylamides, oligo(C_{2-3} alkoxy) C_{2-18} -alkyl(alk)acrylates, and acrylamides, styrene, vinylacetate and N-vinyllactam.

- 42. (new): A composition according to claim 20 in which the said polydispersity is in the range 1.1 to 1.4.
- 43. (new): A composition according to claim 21 in which the said degree of polymerisation is in the range 10 to 100.
- 44. (new): A composition according to claim 22 in which the said degree of polymerisation is in the range 20 to 250.
- 45. (new): A method according to claim 29 in which the biologically active molecule is a cytotoxic compound.
- 46. (new): A method according to claim 29 wherein the hydrophilic block is formed by radical polymerisation of ethylenically unsaturated monomers.
- 47. (new): A method according to claim 46 in which the monomers comprise a zwitterionic monomer.
- 48. (new): A method according to claim 47 in which the zwitterionic monomer has the general formula

Y B X I

in which Y is an ethylenically unsaturated group selected from the group consisting of $H_2C=CR-CO-A-$, $H_2C=CR-C_6H_4-A^1-$, $H_2C=CR-CH_2A^2$, $R^2O-CO-CR=CR-CO-O$, RCH=CH-CO-O-, $RCH=C(COOR^2)CH_2-CO-O$,

$$\bigvee_{N} = \text{and} \qquad \bigvee_{R} = \bigvee_{N} = \bigvee_{$$

A is -O- or NR¹;

 A^1 is selected from the group consisting of a bond, $(CH_2)_IA^2$ and $(CH_2)_ISO_3$ - in which I is 1 to 12;

A² is selected from the group consisting of a bond, -O-, O-CO-, CO-O, CO-NR¹-, -NR¹-CO, O-CO-NR¹- and NR¹-CO-O-;

R is hydrogen or C_{1-4} alkyl;

R¹ is hydrogen, C₁₋₄-alkyl or BX;

 R^2 is hydrogen or C_{1-4} alkyl; and

B is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups, and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents.

49. (new): A method according to claim 49 in which W^+ is a group of formula $-W^1-N^+R^3$, $-W^1-P^+R^4$, $-W^1-S^+R^4$ or $-W^1-Het^+$ in which:

W¹ is selected from the group consisting of alkanediyl of 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene and alkylene cycloalkyl alkylene, which group W¹ optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R³ are the same or different and each is selected from the group consisting of hydrogen, alkyl of 1 to 4 carbon atoms and aryl or two of the groups R³ together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or

the three groups R³ together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R³ is substituted by a hydrophilic functional group, and

the groups R^4 are the same or different and each is R^3 or a group OR^3 , where R^3 is as defined above; and

Het is an aromatic nitrogen-, phosphorus- or sulphur-containing ring.

50. (new): A method according to claim 49 in which X is a group of the general formula II

in which the moieties A^3 and A^4 , which are the same or different, are -O-, -S-, -NH- or a valence bond and W^+ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is a C_{1-12} -alkanediyl group.

51. (new): A method according to claim 48 in which X has the general formula III

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where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4.

- 52. (new): The method according to claim 48 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.
- 53. (new): A method according to claim 29 in which the hydrophobic block comprises pendant groups which are ionisable, having a pK_A or pK_B in the range 4 to 10.
- 54. (new): A method according to claim 53 in which the hydrophobic block is formed by radical polymerisation of ethylenically unsaturated monomers including monomers having the general formula VII

$$Y^{1}B^{1}Q$$
 VII

in which Y^1 is an ethylenically unsaturated group selected from the group consisting of $H_2C=CR^{40}-CO-A^8-$, $H_2C=CR^{14}-C_6H_4-A^9-$, $H_2C=CR^{14}-CH_2A^{10}$, $R^{16}O-CO-CR^{14}=CR^{14}-CO-O$, $R^{14}CH=CH-CO-O-$, $R^{14}CH=C(COOR^{16})CH_2-CO-O$,

 A^{8} is -O- or NR¹⁵;

 A^9 is selected from the group consisting of a bond, $(CH_2)_qA^{10}$ and $(CH_2)_qSO_3$ - in which q is 1 to 12;

A¹⁰ is selected from the group consisting of a bond, -O-, O-CO-, CO-O-, CO-NR⁴¹-, -NR⁴¹-CO, O-CO-NR¹⁵- and NR¹⁵-CO-O-;

 R^{14} is hydrogen or C_{1-4} alkyl;

R¹⁵ is hydrogen, C₁₋₄-alkyl or B¹Q;

 R^{16} is hydrogen or C_{1-4} alkyl;

B¹ is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups, and alkylene (oligooxalkylene) group, optionally containing one or more fluorine substituents; and

Q is a cationic or cationisable group of the formula $-NR^{17}_{P}$, $-PR^{17}_{P}$ or SR^{17}_{r} , in which p is 2 or 3, r is 1 or 2, the groups R^{17} are the same or different and each is selected from the group consisting of hydrogen, C_{1-24} alkyl and aryl, or two of the groups R^{17} together with the heteroatom to which they are attached from a 5 to 7 membered heterocyclic ring or three R^{17} groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring, either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R^{17} groups may be substituted by amino or hydroxyl groups or halogen.

55. (new): A method according to claim 54 in which Q is NR^{17}_{2} in which each R^{17} is H or C_{1-4} alkyl.

56. (new): A method according to claim 46 in which the radical polymerisation is a controlled radical polymerisation.